10/584025

IAP20 Rec'd PCT/PTO 22 JUN 2006

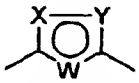
WHAT IS CLAIMED IS:

1. A compound of formula (I), or a pharmaceutically acceptable salt thereof:

$$R^1\text{-}V\text{-}B\text{-}R^2$$

(I)

wherein V represents a 5-membered heteroaryl ring of the formula:



wherein W is N and one of X and Y is N and the other is O;

B is -CH=CH- or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is 2 or 3;

m is independently 0, 1 or 2;

R^1 is 4-pyridyl optionally substituted by 1 or 2 halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl groups;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{1-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-8} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;
R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;
R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;
R^{10} is hydrogen or C_{1-4} alkyl;
R^{11} is phenyl; and
R^{12} is hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl;
provided that the compound is not:

a) 4-(5-piperidin-4-yl-[1,2,4]oxadiazol-3-yl)pyridine;
b) 4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-yl)piperidine-1-carboxylic acid ^{t}butyl ester; or
c) 4-[5-(4-butylcyclohexyl)-[1,2,4]oxadiazol-3-yl]pyridine.

2. A compound according to claim 1, or a pharmaceutically acceptable salt thereof; wherein R^1 is 4-pyridyl optionally substituted by halo, C_{1-4} alkyl, C_{1-4} alkoxy or CN.

3. A compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 is a 4- to 7-membered cycloalkyl substituted by R^3, or 4- to 7-membered heterocyclyl containing one nitrogen atom which is substituted by $C(O)OR^4$.

4. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_{3-8} alkyl which may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl.

5. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, 5- to 6-membered heteroaryl containing one or two nitrogen atoms, C_{1-4} alkylC_{3-7} cycloalkyl or C_{1-4} alkylaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6 and CO_2C_{1-4} alkyl.

6. A compound according to claim 5, or a pharmaceutically acceptable salt thereof, wherein R^4 is C_{3-6} alkyl optionally substituted with up to 5 fluoro or chloro atoms, and which may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl.

7. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^5 is C_{1-4} alkyl.

8. A compound as defined in any one of Examples 1, 3 to 5, 10 to 13, 16 to 39, 41, 42, or 52 to 132, 134,135, or 147 to 149 or a pharmaceutically acceptable salt thereof.

9. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

B is -CH=CH- or $(CH_2)_m$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$ or C(O);

n is 2 or 3;

m is independently 0, 1 or 2;

R^2 is 4- to 7-membered heterocyclyl containing one nitrogen atom which is substituted by $C(O)OR^4$ or a 6-membered nitrogen containing heteroaryl group;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^5)_2$ and NO_2;

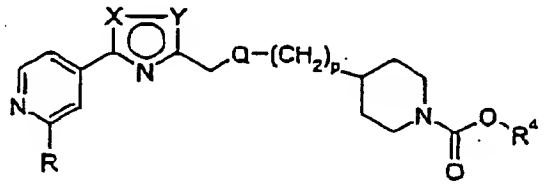
R^5 is hydrogen or C_{1-4} alkyl;

R^6 are independently hydrogen, or C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl; and

R^{10} is hydrogen or C_{1-4} alkyl.

10. A compound according to claim 1 having the formula (Ie), or a pharmaceutically acceptable salt thereof:



(Ie)

wherein one of X and Y is N, and the other is O;

Q is O, NR^5 or CH_2;

R is hydrogen, halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is C_{1-4} alkyl;

R^6 are independently hydrogen, or C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$

may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl; and

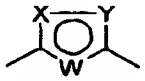
p is 0 or 1.

11. A pharmaceutical composition comprising a compound according to any one of claims 1 to 10, including the compound of proviso c), or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

12. A method for the treatment of a disease or condition in which GPR116 plays a role comprising a step of administering to a subject in need thereof an effective amount of a compound of the formula, or pharmaceutically acceptable salt thereof:

$$R^1\text{-}V\text{-}B\text{-}R^2$$

wherein V represents a 5-membered heteroaryl ring of the formula:



wherein W is N and one of X and Y is N and the other is O;

B is -CH=CH- or $(CH_2)_n$, where one of the CH_2 groups may be replaced by O, NR^5, $S(O)_m$, C(O) or $C(O)NR^{12}$;

n is 0, 1, 2 or 3;

m is independently 0, 1 or 2;

R^1 is 3- or 4-pyridyl, 4- or 5-pyrimidinyl or 2-pyrazinyl, any of which may be optionally substituted by one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-7} cycloalkyl, aryl, OR^6, CN, NO_2, $S(O)_mR^6$, $CON(R^6)_2$, $N(R^6)_2$, $NR^{10}COR^6$, $NR^{10}SO_2R^6$, $SO_2N(R^6)_2$, a 4- to 7-membered heterocyclyl group or a 5- or 6-membered heteroaryl group;

R^2 is 4- to 7-membered cycloalkyl substituted by R^3, $C(O)OR^3$, $C(O)R^3$ or $S(O)_2R^3$, or 4- to 7-membered heterocyclyl, containing one or two nitrogen atoms which is unsubstituted or substituted by $C(O)OR^4$, $C(O)R^3$, $S(O)_2R^3$, $C(O)NHR^4$, $P(O)(OR^{11})_2$ or a 5- or 6-membered nitrogen containing heteroaryl group;

R^3 is C_{3-8} alkyl, C_{3-8} alkenyl or C_{3-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be optionally substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^4 is C_{2-8} alkyl, C_{2-8} alkenyl or C_{2-8} alkynyl, any of which may be optionally substituted with up to 5 fluoro or chloro atoms, and may contain a CH_2 group that may be replaced by O, or C_{3-7} cycloalkyl, aryl, heterocyclyl, heteroaryl, C_{1-4} alkylC_{3-7} cycloalkyl, C_{1-4} alkylaryl, C_{1-4} alkylheterocyclyl or C_{1-4} alkylheteroaryl, any of which may be substituted with one or more

substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^6, CN, CO_2C_{1-4} alkyl, $N(R^6)_2$ and NO_2;

R^5 is hydrogen, $C(O)R^7$, $S(O)_2R^8$, C_{3-7} cycloalkyl or C_{1-4} alkyl optionally substituted by OR^6, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-2} alkyl, C_{1-2} fluoroalkyl, OR^6, CN, $N(R^6)_2$ and NO_2;

R^6 are independently hydrogen C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl, heterocyclyl or heteroaryl, wherein the cyclic groups may be substituted with one or more substituents selected from halo, C_{1-4} alkyl, C_{1-4} fluoroalkyl, OR^9, CN, SO_2CH_3, $N(R^{10})_2$ and NO_2; or a group $N(R^{10})_2$ may form a 4- to 7-membered heterocyclic ring optionally containing a further heteroatom selected from O and NR^{10};

R^7 is hydrogen, C_{1-4} alkyl, OR^6, $N(R^6)_2$, aryl or heteroaryl;

R^8 is C_{1-4} alkyl, C_{1-4} fluoroalkyl, aryl or heteroaryl;

R^9 is hydrogen, C_{1-2} alkyl or C_{1-2} fluoroalkyl;

R^{10} is hydrogen or C_{1-4} alkyl;

R^{11} is phenyl; and

R^{12} is hydrogen, C_{1-4} alkyl or C_{3-7} cycloalkyl.

13. A method for the treatment of a disease or condition in which GPR116 plays a role comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

14. A method for the regulation of satiety comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

15. A method for the treatment of obesity comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.

16. A method for the treatment of diabetes comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 10 or 12, including the compounds of provisos a) to c), or a pharmaceutically acceptable salt thereof.